

Applicant: Cy A. Stein et al.
Serial No.: 09/753,169
Filed: January 2, 2001
Page 4

A4 cont'd were stripped of radioactivity and reprobed with a ^{32}P -labeled G3PDH probe to confirm the equal loading. --

A marked up copy of the amendments to the brief description of the figures and the specification is attached hereto as **Exhibit A**.

REMARKS

Applicants have amended the specification to insert sequence identifiers as necessary. Applicants maintain that the amendments to the specification raise no issue of new matter. Applicants, therefore, respectfully request entry of this Amendment.

In the September 26, 2002 Office Action, the Examiner stated that the above-identified application fails to comply with 37 C.F.R. §1.821 through §1.825. A copy of the Office Action is attached hereto as **Exhibit B**.

In response, applicants have amended the specification to insert sequence identifiers where necessary. In addition, applicants submit as **Exhibit C** attached hereto a Paper Copy Sequence Listing, a Statement in Accordance with 37 C.F.R. §1.821(f) as **Exhibit D**, and a C.R.F. Sequence Listing.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorneys invite the Examiner to telephone them at the number provided below.

Applicant: Cy A. Stein et al.
Serial No.: 09/753,169
Filed: January 2, 2001
Page 5


No fee is deemed necessary in connection with the filing of this Amendment. If any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents
BOX Sequence, P.O. 2327
Arlington, VA 22202

 10/17/02
Peter J. Phillips /Date
Registration No. 29,691

John P. White
Registration No. 28,678
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Registration No. 29,691
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Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
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Mark-up Version to Show Changes Made

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In the Brief Description of Figures:

The Figure description starting page 5, line 2 has been amended as follows:

--Figure 1

Oligonucleotide sequences complementary to bcl-X_L mRNA; A (SEQ ID NO:1), B (SEQ ID NO:2), C (SEQ ID NO:3), D (SEQ ID NO:4), E (SEQ ID NO:5), F (SEQ ID NO:6), G (SEQ ID NO:7), H (SEQ ID NO:8), I (SEQ ID NO:9), J (SEQ ID NO:10), K (SEQ ID NO:11), L (SEQ ID NO:12), M (SEQ ID NO:13).---

The Figure description starting page 5, line 5 has been amended as follows:

--Figures 2A and 2B

Oligonucleotide sequences and analogs thereof complementary to bcl-X_L mRNA; Figure 2A shows: A (SEQ ID NO:14), A' (SEQ ID NO:15), B (SEQ ID NO:16), C (SEQ ID NO:17), C' (SEQ ID NO:18), D (SEQ ID NO:19), E (SEQ ID NO:20), E' (SEQ ID NO:21), F (SEQ ID NO:22), G (SEQ ID NO:23), G' (SEQ ID NO:24); Figure 2B shows, H (SEQ ID NO:25), H' (SEQ ID NO:26), I (SEQ ID NO:27), I' (SEQ ID NO:28), J (SEQ ID NO:29), K (SEQ ID NO:30), K' (SEQ ID NO:31), L (SEQ ID NO:32), L' (SEQ ID NO:33), M (SEQ ID NO:34), M' (SEQ ID NO:35).---

The Figure description starting page 6, line 2 has been amended as follows:

--Figure 10

Most active chimeric PS-PO oligonucleotides by their ability to down-regulate Bcl-XL protein expression (from top to bottom SEQ ID NO:15; SEQ ID NO:19; SEQ ID NO:24; SEQ ID NO:27; SEQ ID NO:22; SEQ

In the Specification:

The paragraph starting page 22, line 33 has been amended as follows:

--Two clones of LNCaP cells overexpressing bcl-xL protein (1072-4 and 1072-5) have been obtained after transfection of wild type LNCaP cells with the plasmid vector pSFFV/bcl-xL and lipofectin. Also a mock transfectant clone of LNCaP cells carrying neo[®] resistance gene (1072-3) was used for the control experiments. Clone 1072-4 demonstrates 10-fold overexpression, and clone 1072-5 - 4-fold overexpression of bcl-xL protein. Western blot analysis for bcl-xL protein was performed as described above. Results for bcl-xL protein expression were confirmed by Northern blot analysis for bcl-xL mRNA expression, demonstrating significant elevation of this mRNA in bcl-xL transformed cell lines. For the Northern blot analysis, the total RNA was isolated from the cells using TRIZOL reagent (GIBCO BRL), and 20 µg aliquotes were separated in RNA-formaldehyde gel, blotted onto nylon membranes (Schleicher & Schull), UV-linked and prehybridized for two hours at 42 °C in the standard hybridization solution. Then the blot was hybridized overnight with the PCR-amplified fragment of human bcl-xL cDNA at 42 °C. Bcl-xL coding fragment was amplified from pSFFV/bcl-xL plasmid using bcl-x specific primers. The primer sequences were: bcl-x-upstream, 5'-ATGTCTCAGAGCAACCGGGA-3' (SEO ID NO:36); and bcl-x-downstream, 5'-TCATTTCCGACTGAAGAGTG-3' (SEO ID NO:37). Twenty five cycles of amplification were performed in DNA Thermal Cycler (Perkin-Elmer, Norwalk, CT) at 94 °C (30 sec), 55 °C (30 sec), and 72 °C (30 sec). The PCR products were analysed on a 1.2% agarose gel. The resultant fragment was labeled by random primer method to the specific activity 10⁷ cpm/ng of the probe and used for the hybridization. After washings blots were autoradiographed for 24h

at -80 °C. Blots were stripped of radioactivity and reprobed with a ^{32}P -labeled G3PDH probe to confirm the equal loading.--



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United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,169	01/02/2001	Cy A. Stein	55669-A-PCT-US/JPW/GJC	9695

7590 09/26/2002

John P. White
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER

MCGARRY, SEAN

ART UNIT PAPER NUMBER

1635

DATE MAILED: 09/26/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

OCT 22 2002
PATENT & TRADEMARK OFFICE

Application No.

09/753,169 ✓

Applicant(s)

STEIN ET AL

Examiner

Sean McGarry

Art Unit

1635

Office Action Summary

OCT 1 - 2002

COPY

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 137).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

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Status

OCT 24 2002

- 1) ☒ Responsive to communication(s) filed on 19 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

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Disposition of Claims

- 4) ☐ Claim(s) _____ is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

1m. 10.26.02
 2m. 11.26.02
 3m. 12.26.02
 4m. 1.26.03
 5m. 2.26.03
 6m. 3.26.03 - AP

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Notice to Comply Requirements*

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Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/753,169			


EXAMINER	
McGarry	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED:

Please find below a communication from the EXAMINER in charge of this application

Commissioner of Patents

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CAR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **It is noted that applicant filed a CRF on 3/19/02, however, no CRF has been entered for the instant application. It is requested that applicant provide a new sequence disk. It is also noted that Figures 1-3, and 10 disclose sequences that do not have the required Sequence identifiers in the "Brief Description of the Drawings" section of the specification or in the Figures themselves.**
2. Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CAR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CAR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CAR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.
3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean McGarry whose telephone number is (703) 305-7028. The examiner can normally be reached on Monday-Thursday from 6:00-4:30 pm.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached at (703) 308-0447. The FAX phone number for group 1600 is (703)308-4242.
An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is (703)308-0196.


SEAN MCGARRY
PRIMARY EXAMINER
1635- 7/25/02

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: _____

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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OCT 24 2002

14/A

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SEQUENCE LISTING

<110> The Trustees of Columbia University In The City of New York

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Dkt. 0575/55669-A-PCT-US/JPW/PJP/BJA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#14

Applicant : Cy A. Stein et al.

Serial No.: 09/753,169

Examiner: S. McGarry

Filed : January 2, 2001

Group Art Unit: 1635

For : OLIGONUCLEOTIDE INHIBITORS OF bcl-xL

1185 Avenue of the Americas
New York, New York 10036
October 17, 2002

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Assistant Commissioner for Patents
BOX Sequence, P.O. 2327
Arlington, VA 22202

SIR:

STATEMENT IN ACCORDANCE WITH 37 C.F.R. §1.821(f)

In accordance with 37 C.F.R. §1.821(f), I hereby certify that the computer readable form containing the nucleic acid and/or amino acid sequences required by 37 C.F.R. §1.821(e) and submitted herewith contains the same information as the written "Sequence Listing" (26 pages) (Exhibit C) that is submitted herewith.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

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